

## REMARKS

### I. Status of the Claims

New claims 62–68 are now pending in Applicants' application, claims 58–61 having been cancelled without prejudice or disclaimer. Applicants reserve the right to file one or more continuing applications directed to the cancelled subject matter.

Following an interview conducted with Primary Examiner Scott Priebe and Examiner Ram Shukla on January 5, 2001, Applicants have cancelled previously pending claims 58–61 and substituted new claims 62–68. In the interview, Applicants submitted a proposed claim containing an amendment to previously pending claim 58. This proposed claim modified claim 58 to contain a step directed to screening the cell for a phenotype wherein the phenotype is expression of the endogenous gene or is induced by expression of the gene. In the interview, the Examiners indicated that such an amendment would be dispositive in overcoming the rejection under 35 U.S.C. § 112 which was set forth in the Office Action dated April 28, 2000. Accordingly, new claim 62 encompasses the subject matter of proposed claim 58 by providing step (c) that involves screening the cells for a cell in which a desired gene is activated or screening the cells for a cell with a desired phenotype, where the phenotype is induced by expression of the activated gene. Support for screening the cells for expression of the activated gene or for a phenotype induced by expression of the activated gene can be found in Applicants' specification, *inter alia*, on page 31, lines 13–14, and on pages 65–67.

Previously pending claim 59 has been replaced with new claim 63. In the interview, regarding claim 59, the Examiners suggested introducing a step wherein the gene product is secreted into the cell culture medium and wherein screening is for a cell from which the gene product is secreted. Accordingly, new claim 63 replaces claim 59 wherein step (b) has been

amended to recite (1) that the cells containing the activation vector are cultured in reduced-serum cell culture medium under conditions favoring production of a protein encoded by the activated gene and (2) secretion of the protein into the cell culture medium. Step (c) now recites that in the method the cells containing the activation vector are screened for a cell in which a desired gene is activated and the protein encoded by this gene is secreted into the cell culture medium. Support for secretion of the gene product of the activated gene can be found in Applicants' specification, *inter alia*, on pages 65, line 3, page 65, the section entitled "ELISA," and the paragraph spanning pages 44–45. As suggested by the Examiners, the claims have also been amended to recite that screening is for a "desired" gene or a "desired" phenotype. Support for this amendment can be found in Applicants' specification, *inter alia*, on pages 65–67. New claims 66 and 67 have been added to recite that the vector contains a transcriptional regulatory sequence by means of which the endogenous gene is activated. Support for this amendment can be found throughout Applicants' specification, for example, on page 6, first paragraph. Finally, new claim 68 recites that the vector integrates into the genome by non-homologous recombination. Support for this amendment can be found throughout Applicants' specification, for example, in the first full paragraph of page 6 and page 30. Accordingly, no new matter has been added with these amendments.

## II. Miscellaneous

### The Interview

On January 5, 2001, inventor John Harrington and Applicants' attorney, Anne Brown, conducted an interview with Examiners Shukla and Priebe. Applicants thank the Examiners for the helpful discussion to resolve issues set forth in the Office Action dated November 17, 2000. In accordance with the Examiners' suggestions, Applicants have made every effort to present amendments to claims 58 and 59. New claim 62 replaces claim 58 and is directed to

embodiments whereby the cells are screened for the activated gene or are screened for a phenotype induced by expression of activated gene. The new replacement claims also recite that screening is for a “desired” gene or phenotype. Furthermore, the replacement claim for claim 59 (claim 63) has been amended to recite that the activated gene product is secreted into the culture medium wherein screening is performed for a desired gene product.

III. The Rejections in the Final Office Action dated November 17, 2000

In the final Office Action, the Examiner maintained the rejection under 35 U.S.C. § 112, first paragraph, “for reasons of record set forth in the previous Office Action.” Applicants discussed the maintenance of this rejection in the interview. In the interview, the Examiner indicated that the rejection of claim 58 could be overcome by amending the claim to recite that the cells containing the activation vector are screened for expression of a desired activated gene or a desired phenotype induced by expression of the activated gene. Based on the amendment, Applicants believe that the rejection of claim 58 (replaced by new claim 62) has been addressed and overcome.

Regarding claim 59, the Examiners further indicated that a step wherein the activated gene product is secreted is not evident. Therefore, a claim is presented that recites a step wherein a cell is screened for a protein that is secreted into the medium. Accordingly, Applicants believe that the rejection of claim 59 (replaced by new claim 63) has been addressed and overcome.

Applicants also raised the issue of enablement for genome-wide activation. It is not clear if the rejection on this ground has been maintained in the final Office Action. Explicit clarification is requested. Although Applicants presented extensive argument and

Declaratory evidence on the issue, this argument and evidence was not explicitly addressed by the Examiner. This issue was also raised in U.S. Patent Application No. 09/276,820, where Applicants also presented the arguments and evidence cited above. The rejection on this ground was not maintained in that case. Furthermore, the Examiners indicated that this issue would be moot with the suggested amendments in the present case. Accordingly, Applicants believe that this ground for rejection is overcome in view of Applicants' arguments and amendments.

In the interview, Applicants also discussed the rejection on the grounds of alleged inoperability of truncated gene products. The Examiners recognized that the claims as amended inherently include truncated gene products that are functional in the claimed method. Therefore, the Examiners indicated that this issue is moot in view of the suggested amendments.

Applicants also discussed the issue of the enablement of concentrating and purifying a protein. In the interview, the Examiners indicated that this aspect was no longer an issue.

Applicants also discussed the issue of correlation of a phenotype with a disease. The Examiners also indicated that this aspect was no longer an issue.

### **CONCLUSION**

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding

Office Action and, as such, the present application is in condition for allowance. If the Examiner believes that a telephone discussion regarding these claims would be helpful, he is invited to telephone Applicants' attorney, Anne Brown, at (216) 426-3586. Prompt and favorable consideration of this Response is respectfully requested.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 CFR §1.136(a), and any fees required therefor are hereby authorized to be charged to Deposit Account No. 50-0622, referencing Attorney Docket No. 0221-0003L.

Respectfully submitted,

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